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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/513,086 | 02/24/2000 | Linda S. Mansfield | MSU 4.1-458 | 4724 |

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|---|---|
| WOITACH, JOSEPH T | |
| ART UNIT | PAPER NUMBER |
| 1632 | 12 |

DATE MAILED: 03/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/513,086 | Applicant(s) MANSFIELD ET AL. | |
|---|---|---|---|
| | Examiner Joseph Woitach | Art Unit 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *4-9,13-17,46,49 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9,13-17,46,49 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

This application is an original application filed February 24, 2000, which claims benefit to provisional application 60/152,193, filed September 2, 1999.

Applicants amendment filed January 3, 2002, paper number 11 has been received and entered. Claims 23-28 have been canceled. Claims 4, 13 and 45 have been amended. Claims 4-9, 13-17, 45, 46, 49 and 50 are pending and currently under examination.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-9, 13-17, 45, 46, 49 and 50 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants point out the amendments to the claims, and indicate that the instant specification provides methods for isolating *Sarcosystis neuron,* and identification of the 16 and 30 kDa proteins on a 2-D gel. Further, Applicants argue that the identification of the antigens can also be found in Mansfield *et al.*, US Patent 6,153,394 which was incorporated by reference.

In light of these teachings, Applicants argue that it would not be undue burden to produce the vaccine as instantly claimed. See Applicants' amendment, pages 4-5. Applicants arguments have been fully considered, but not found persuasive.

The basis of the instant rejection is the lack of written description for the 16 and 30 kDa *Sarcosystis neurona* antigens, not if one could make a vaccine comprising these antigens. As pointed out in the previous office action, the claims encompass a vaccine comprising at least one epitope of a recombinant polypeptide consist of one epitope of a 16(±4) kDa antigen and one epitope of a 30(±4) kDa antigen and methods of making said recombinant protein, and neither the present specification nor the art of record provide the polypeptide or polynucleotide sequences for the epitope of the 16(±4) kDa antigen and the 30(±4) kDa antigen. Based on the evidence of record, these sequences have not been identified nor described. Therefore, in order to practice the invention as claimed the artisan must first obtain the polypeptide and/or polynucleotide sequences of the 16(±4) kDa antigen and the 30(±4) kDa antigen. Examiner agrees that the specification provides the general methods of cloning cDNA sequences from expression libraries, however, the sequences obtained by this method are not disclosed. Thus, the specification fails to provide any detail to any of the sequences of the 16(±4) kDa antigen or the 30(±4) kDa antigen. The written description of a claim is evaluated on the basis of the claimed invention as a whole, and case law establishes that the requirement for written description relates to the subject matter defined by the claims. *In re Wright*, 9 USPQ2d 1649 (Fed. Cir. 1989). In the instant case, though Examiner would agree that antibodies exist which

recognize a 16(±4) kDa antigen or a 30(±4) kDa antigen, it is maintained that no specific sequence which is recognized by these antibodies is disclosed. The claimed invention is directed to vaccine comprising at least one epitope of a recombinant polypeptide consist of one epitope of a 16(±4) kDa antigen and one epitope of a 30(±4) kDa antigen and methods of making said recombinant protein, however the specification fails to demonstrate possession of the invention in adequate detail to satisfy the written description requirement. The skilled artisan cannot envision the detailed structure of the claimed antigens/vaccine, nor the materials necessary to practice the methods steps necessary to carry out the claimed methods of generating recombinant protein which would serve as an antigen/vaccine, and thus, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. For example, if a particular sequence for a 16 or 30 kDa protein were disclosed today, given the lack of written description in the instant disclosure, or the art of record at the time of filing, one could not determine if the newly disclosed sequence(s) would be encompassed by the instant claims. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Further, case law has established that one cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Therefore, it is maintained that the polypeptide and polynucleotide sequences needed to make and use the claimed invention do meet the written description provision of 35 U.S.C. §112,

first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 4-9, 13-17, 45-46, 49 and 50 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants' note the amendments to the claims to encompass 'therapeutic vaccines and methods of preventing disease caused by *Sarcosystis neurona*' and no longer encompasses preventing infection. Applicants summarize the teachings of Liang *et al.* and argue that unlike the limitations Examiner has pointed out in the teachings of Liang *et al.* which are directed to reducing parasite production *in vivo*, the present invention is directed to preventing the parasite form entering the central nervous system. Applicants point out that Liang *et al.* teach that EPM occurs only after the merozite crosses the blood-brain barrier into the central nervous system, and argue that in light of this statement, Applicants' instantly claimed vaccine would be effective in preventing disease caused by the parasite. See Applicants amendment, pages 5-7. Applicants' amendments have been fully considered, but not found persuasive.

As noted in the previous office action, the court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The court continues to say that "tossing out the mere germ of an idea does

not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genentech inc v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005). As noted above, the 35 USC 112, first paragraph, rejection for lack of written description, the instant specification does not even provide the guidance to what the sequences for the 16 and 30 kDa proteins/polynucleotides are. Absent any specific sequences for these antigens, how would the artisan define epitopes which would be effective in generating neutralizing antibodies. The high degree of unpredictability associated with the claimed method underscores the need to provide teachings in the specification that would provide the artisan with specific treatment regimens that achieve a therapeutic benefit, and none of the sequences for either the 16(±4) kDa antigen or the 30(±4) kDa antigen are disclosed. Absent this information, the artisan would not know what polypeptides or polynucleotides one would use to begin to generate the claimed invention. Further, as indicated by Liang *et al.*, one cannot predict the activity of an antigen for use in a vaccine from *in vitro* data. While the immunological data of record suggests that the antigens are cell surface antigens, there is no function ascribe to these antigens and thus, no nexus between targeting these antigens and disrupting any activity which would result in protective effect required of a vaccine. Without necessary specific guidance in the specification and the lack of correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan. Examiner would agree that a particular neutralizing antibody given in large enough amounts may be effective in

reducing the progression of diseases caused by the infection of the central nervous system, however the instant specification fails to support any particular or specific sequence of the 16 and 30 kDa proteins would serve as such an epitope. Examiner would agree that the general statement of Liang *et al.* provides a suggestion and motivation to inhibit the spread of the parasite to the central nervous system which was recognized by the skilled artisan at the time of the claimed invention, however the instant disclosure does not teach the necessary materials nor specific methodology to accomplish this proposal.

In addition, as noted in the previous office action, a vaccine is a preparation intended for active immunological prophylaxis. Applicants state that the present vaccine does not prevent the *Sarcocystis neurona* from infecting the equine (page 3; first full paragraph, first line), however the claims still encompass this limitation through the use of the word vaccine in the instant claims. The new amendments to the claims to recite that the vaccine prevents diseases caused by *Sarcocystis neurona* infection does not further limit away from the fact that a vaccine, as defined by the art, would encompass a preparation intended for active immunological prophylaxis (see Stedman's Medical Dictionary as it defines a vaccine). Furthermore, though Examiner would agree that an antigen may serve as a vaccine generating neutralizing antibodies and possibly also prevent the spread of the parasite, in light of the teaching of Liang *et al.* it is clear that not all antibodies generated to an antigen will neutralize function of said protein. As pointed to in the previous office action, Liang *et al.* teach that '[A]lthough *S. neurona* was sensitive to specific antibodies, a 10-min exposure to antiserum was required to yield a

significant reduction in parasite production (data not shown). This may partially explain why protective antibodies to some apicomplexan parasites are effective *in vitro* but not *in vivo* (23). Newly released parasites are exposed to serum for a shorter time *in vivo*, and the access of neutralization-sensitive epitopes to antibody may be limited (31).' (page 1837, bottom of first column). The results of and conclusion by Liang *et al.* clearly indicates that *in vitro* data does not necessarily correlate to or be extendable to *in vivo*. Further, Applicants admit that the present invention does not prevent infection of equine, but may prevent the spread of *S. neurona* to the nervous system and CSF. Applicants have proposed that it is plausible that the instantly claimed antigens may serve as a vaccine, however the specification does not provide the necessary guidance nor evidence that the invention prevents the spread of *S. neurona* to the nervous system and CSF which support such an assertion. In light of the teachings of both Liang *et al.* and Kisthardt *et al.* demonstrating the presence of antisera reactivity in most horses tested, and the specific teaching of Liang *et al.* that the ability of an antibody to function *in vitro* does not correlate to function *in vivo,* the instant specification has not provided the necessary teaching to provide a nexus between the proposed antigens which are only defined by molecular weight and a functional vaccine. As previously discussed, there has not been a successful vaccine produced for *S. neurona*, and the instant disclosure has not described nor provided examples of how the recited vaccine differs from those previously found in the art.

Thus, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have

required undue experimentation to practice the full scope of the invention as claimed. Therefore, for the reasons above and of record, and therefore, the rejection is maintained.

***Conclusion***

No claim is allowed. As noted in the previous office action, claims 4-9, 13-17, 45-46, 49 and 50 are free of the prior art of record because the art fails to teach a recombinant polypeptide consisting of one epitope of a 16(±4) kDa antigen and one epitope of a 30(±4) kDa antigen, and use of said polypeptide as a vaccine, however the claims are subject to other rejections.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Patsy Zimmerman whose telephone number is (703)308-8338.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630